REMARKS

Claims 1-13 and 24 have been cancelled. Claims 14, 20, 23, and 25-26 have been amended. Claims 14-23 and 25-26 are now pending in this application. Support for the amendments is found in the existing claims and the specification as discussed below. Accordingly, the amendments do not constitute the addition of new matter. Applicant respectfully requests the entry of the amendments and reconsideration of the application in view of the amendments and the following remarks.

Rejection under 35 U.S.C. § 112, first paragraph – written description

Claims 8-11, 20-22, 24, and 26 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time that the application was filed.

This ground of rejection is moot with respect to claims 8-11 and 24 which have been cancelled.

Claims 20 and 26 have been amended to "(a) a peptide comprising an amino acid sequence consisting of the sequence shown as SEQ ID NO: 2" and "(c) a peptide comprising an amino acid sequence consisting of the sequence shown as SEQ ID NO: 3". Accordingly, claims 20-22, and 26 are limited to peptides which include the sequences of SEQ ID NOS: 2 and /or 3 (which are equivalent to amino acids 36-60 or 36-61, respectively, of SEQ ID NO: 1) which the Examiner has indicated have written description support in the specification. (Office Action, page 4, lines 3-4).

In view of Applicants' amendments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

Rejection under 35 U.S.C. § 112, first paragraph – scope

Claims 8-11, 20-22, 24 and 26 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for peptides consisting of aa residues 36-60 of SEQ ID NO: 1 and aa 36-61 of SEQ ID NO: 1, does not reasonably provide enablement for peptides having substitutions, deletions, additions or inversions of one or more amino acid residues in aa residues of 36-60 of SEQ ID NO: 1 and aa 36-61 of SEQ ID NO: 1.

This ground of rejection is moot with respect to claims 8-11 and 24 which have been cancelled.

As mentioned above, SEQ ID NOS: 2 and 3 are equivalent to amino acids 36-60 or 36-61, respectively, of SEQ ID NO: 1. The claims have been amended to peptides with "an amino acid sequence consisting of the sequence shown as SEQ ID NO: 2" and/or "an amino acid sequence consisting of the sequence shown as SEQ ID NO: 3". The claims have been limited to subject matter which the Examiner considers to be enabled.

In view of Applicants' amendment, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 13, 23, and 25-26 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This ground of rejection is moot with regards to claim 13 which has been cancelled.

Claims 23, 25, and 26 have been amended to recite that the antibody drug and/or complement is also administered and that the lactoferrin hydrolysate is administered before or after administration of the antibody drug and/or complement or simultaneously with the antibody drug and/or complement. Support is found in the specification at page 20, second full paragraph. Accordingly, it is clear that the antibody drug is also administered.

In view of Applicants' amendment, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

Rejection under 35 U.S.C. § 102(a)

Claims 1-11 and 14-26 are rejected under 35 U.S.C. § 102 (a) as being anticipated by Sakurai, et al.(Rinsho Ketsueki (8/30/04) vol. 45, page 915) as evidenced by Yoo, et al. (Jpn .J. Cancer Res., 88: 184 (1977).

A verified translation of Applicants' priority document is submitted herewith to overcome this rejection.

In view of Applicants' submission of the verified translation, withdrawal of the above ground of rejection is respectfully requested.

Rejections under 35 U.S.C. § 102(b)

1) Claims 8-11 and 24 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Nuijens, et al. (US 6333311) or Tomita, et al. (US 5304633).

2) Claims 1-7 are rejected under 35 U.S.C. § 102(b) as being anticipated by JP 2000-229881.

3) Claims 1-11 and 24 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Yoo, et al. (Jpn. J. Cancer Res. 88: 184 (1997) as evidenced by page 12 of Applicants' specification.

4) Claims 1-13 and 24 are rejected under 35 U.S.C. § 102(b) as being anticipated by JP 08-073499.

The above grounds of rejection are moot in view of Applicants' cancellation of claims 1-13 and 24. Withdrawal of the above rejections is respectfully requested.

Rejection under 35 U.S.C. § 102(b)

Claims 8, 10-11, 20, 22 and 26 are rejected under 35 U.S.C. § 102 (b) as being anticipated by WO 00/12542.

This rejection is moot with regards to claims 8 and 10-11 which have been cancelled.

The Examiner asserts that LFB(17-41) of WO 00/12542 reads on SEQ ID NO: 2 of Applicants. The claims have been amended to "...(a) a peptide comprising an amino acid sequence consisting of the sequence shown as SEQ ID NO: 2...". WO 00/12542 does not teach a sequence that consists of the sequence of SEQ ID NO: 2. Accordingly, the claims as amended are not anticipated by WO 00/12542.

Furthermore, claims 20 and 26 have been amended so that the drug composition also includes a complement. Support for the amendment is found in the specification at page 6, line 8, page 10, 3rd line from bottom, page 13, first full paragraph, and Test Examples 1-5 of the specification.

As discussed in the present specification, cytotoxic activity of a complement and/or an antibody drug to kill or injure target tumor cells is enhanced by the ability of the claimed lactoferrin peptides to recover cytotoxic activity of the complement and/or the antibody drug. That is, the presently claimed invention is directed to the use of both the antibody drug together with complement together with a lactoferrin hydrolysate to enhance the anti-tumor effects which is not taught by WO 00/12542.

In view of Applicants' amendments and arguments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

Rejection under 35 U.S.C. § 102(b)

Claims 1-11, 14-17, 19-20, and 22-26 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Iigo, et al. (Clinical and Experimental Metastasis, vol. 17, p. 35 (1999)) as evidenced by Yoo, et al. (Jpn. J. Cancer Res. 88: 184 (1997)).

This rejection is moot with regards to claims 1-11 and 24 which have been cancelled.

Claims 14, 20, 23, 26 and 26 been amended so that the drug composition also includes a complement. Support for the amendment is found in the specification at page 6, line 8, page 10, 3rd line from bottom, page 13, first full paragraph, and Test Examples 1-5 of the specification.

As discussed above, cytotoxic activity of a complement and/or an antibody drug to kill or injure target tumor cells is enhanced by the ability of the claimed lactoferrin peptides to recover cytotoxic activity of the complement and/or the antibody drug. That is, the presently claimed invention is directed to the use of both the antibody drug together with complement together with a lactoferrin hydrolysate to enhance the anti-tumor effects.

Iigo, et al. do not teach Applicants' claimed drug combination. While Table 3 of Iigo, et al. teaches antibody plus complement, a lactoferrin hydrolysate is not included in the treatment. Instead Iigo, et al. teach addition of WBCs which have been harvested from mice treated with bovine lactoferrin (bLF). Clearly, this is a different treatment than claimed by Applicants which is reflected in the different results achieved by Iigo, et al. (compare Table 3 of Iigo, et al. to Test Examples 1-5 of the present specification). In Iigo, et al. the best results are achieved by addition of WBC alone. Addition of anti-CD4mAb or anti-asialoGM1 and/or Complement (rC or gC) does not decrease the survival rate of the cancer cells. In fact, more cancer cells survive when

both the anti-tumor drug and the complement are added (see Groups 5 and 7). Accordingly, Iigo, et al. actually teach away from the claimed invention. In contrast, Applicants show a synergistic effect by combination of anti-tumor drug, complement and lactoferrin hydrolysate as shown in Test Examples 1-5 and discussed further below.

In view of Applicants' amendments and arguments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

Claims 1-22 and 24 are rejected under 35 U.S.C. § 103(a) as being unpatentable over JP 08-073499 in view of Applicants' specification at pages 2, lines 3+.

The ground of rejection is moot with respect to claim 24 which has been cancelled.

The Office Action asserts that the only difference between the claimed invention and the reference is the use of an anti-cancer antibody, that the specification admits that anti-cancer antibodies are known and that it is prima facie obvious to combine two compositions known in the art to be useful for the same purpose.

JP 08-073499 teach mitogen activity of enzymatic decomposition production of lactoferrin and protective activity of enzymatic decomposition production of lactoferrin against virus infection. In contrast, Applicants claimed invention is directed to cytotoxic activity of a complement and/or an antibody drug to kill or injure target tumor cells which is enhanced by the ability of the claimed lactoferrin peptides to recover cytotoxic activity of the complement and/or the antibody drug. That is, the presently claimed invention is directed to the use of both the antibody drug together with complement together with a lactoferrin hydrolysate to enhance the anti-tumor effects which is not taught by JP 08-073499..

Furthermore, while the Examiner asserts that it is prima facie obvious to combine compositions known in the art to be useful for the same purpose, when considering obviousness of a combination of known elements, the operative question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." M.P.E.P. 2141 citing *KSR International Co. v. Teleflex Inc. (KSR),* 550 U.S. ___, 82 USPQ2d 1385 (2007), 1396.

In the present case, the claimed invention demonstrates an unexpected effect based upon the data provided in the specification. For example, Table 1 at page 31 shows cytotoxic activity of the drug combination according to the claimed invention applied against human Burkitt lymphoma Raji cells. When the sample includes the lactoferrin peptide only, cytotoxic activity was 1.0 to 1.2% (Last row, columns 1 & 2; note Test Sample includes lactoferrin hydrolysate and Control sample includes a dilution, see page 28, 3rd full paragraph). When the sample includes the antibody drug plus complement (minus lactoferrin), the cytotoxic activity was 30.7% (row 1, last column). When the lactoferrin hydrolysate is combined with the antibody drug and the complement, cytotoxic activity was 45.7% (col. 1, row 1). As the additive effect of the lactoferrin plus the antibody drug complement would be expected to be about 32% (30.7% + 1-1.2%), the results actually achieved were unexpected. Similar results are shown in Test Examples 2-5. Accordingly, Applicants have demonstrated an unexpected result which could not have been predicted from the cited reference.

In view of Applicants' amendments and arguments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

Claims 1-11, and 14-26 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Iigo, et al. (Clinical and Experimental Metastasis vol. 17, page 35 (1999)) in view of Yoo, et al. (Jpn. J. Cancer Res. 88: 184(1997)), WO 00/12542, JP 2000-229881, and Applicants' admission on page 2, lines 3-13.

This rejection is moot with regards to claims 1-11 and 24 which have been cancelled.

As discussed above, Claims 14, 20, 23, 26 and 26 been amended so that the drug composition also includes a complement. Support for the amendment is found in the specification at page 6, line 8, page 10, 3rd line from bottom, page 13, first full paragraph, and Test Examples 1-5 of the specification.

Applicants have shown that cytotoxic activity of a complement and/or an antibody drug to kill or injure target tumor cells is enhanced by the ability of the claimed lactoferrin peptides to recover cytotoxic activity of the complement and/or the antibody drug. That is, the presently

claimed invention is directed to the use of both the antibody drug together with complement together with a lactoferrin hydrolysate to enhance the anti-tumor effects.

Iigo, et al. do not teach Applicants' claimed drug combination. While Table 3 of Iigo, et al. teaches antibody plus complement, a lactoferrin hydrolysate is not included in the treatment. Instead Iigo, et al. teach addition of WBCs which have been harvested from mice treated with bovine lactoferrin (bLF). Clearly, this is a different treatment than claimed by Applicants which is reflected in the different results achieved by Iigo, et al. (compare Table 3 of Iigo, et al. to Test Examples 1-5 of the present specification). In Iigo, et al. the best results are achieved by addition of WBC alone. Addition of anti-CD4mAb or anti-asialoGM1 and/or Complement (rC or gC) does not decrease the survival rate of the cancer cells. In fact, more cancer cells survive when both the anti-tumor drug and the complement are added (see Groups 5 and 7). Accordingly, Iigo, et al. actually teach away from the claimed invention. In contrast, Applicants show a synergistic effect by combination of anti-tumor drug, complement and lactoferrin hydrolysate as shown in Test Examples 1-5 and discussed further below.

Neither WO 00/12542 nor JP 2000-229881 correct this deficiency as neither reference teaches the use of complement in combination with an antibody drug and a lactoferrin hydrolysate. Accordingly, the references taken as a whole do not teach all of the elements of the claimed invention.

The Office Action asserts that it would have been obvious to combine anti-cancer treatments for their known and expected benefits. In response, Applicants point to the data presented in the specification that provides evidence of unexpected results. As stated above, Table 1 at page 31 shows cytotoxic activity of the drug combination according to the claimed invention applied against human Burkitt lymphoma Raji cells. When the sample included the lactoferrin peptide only, cytotoxic activity was 1.0 to 1.2% (Last row, columns 1 & 2; note Test Sample includes lactoferrin hydrolysate and Control sample includes a dilution, see page 28, 3rd full paragraph). When the sample includes the antibody drug plus complement (minus lactoferrin), the cytotoxic activity was 30.7% (row 1, last column). When the lactoferrin hydrolysate is combined with the antibody drug and the complement, cytotoxic activity was 45.7% (col. 1, row 1). As the additive effect of the lactoferrin plus the antibody drug

complement would be expected to be about 32% (30.7% + 1-1.2%), the results actually achieved (45.7%) were unexpected. Similar results are shown in Test Examples 2-5.

Accordingly, the cited references taken as a whole do not teach all of the elements of the claimed invention. None of the cited references teach use of complement except for Iigo, et al. Iigo, et al, in this respect, teaches away from the claimed invention. Furthermore, the administration of the antibody drug + complement + lactoferrin hydrolysate demonstrates a synergistic effect.

In view of Applicants' arguments and amendments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, the Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. The Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that the Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

Co-Pending Applications of Assignee

Applicant wishes to draw to the Examiner's attention to the following co-pending applications of the present application's assignee. Item in **BOLD** is the present application.

Serial Number	Title	Filed
10/110,972	METHOD OF DETECTING AND IDENTIFYING THICKNESS OF SHEET-LIKE FOOD, METHOD OF MANUFACTURING SHEET-LIKE FOOD, AND DEVICES THEREFOR	04/18/02
10/432,551	INTERFERON THERAPEUTIC EFFECT-POTENTIATING AGENTS	05/23/03
10/451,587	INTERLEUKIN-18 INDUCING AGENT	06/23/03

10/492,306	METHOD OF PRESERVING FOOD, AND METHOD OF PRODUCING NON-FROZEN WATER	04/12/04
10/709,674	BIFIDOBACTERIUM LONGUM	05/21/04
10/510,088	CYSTEINE PROTEASE INHIBITOR	10/04/04
10/513,523	PROTEASE INHIBITOR	11/04/04
10/518,018	INTERLEUKIN-6 SUPPRESSIVE AGENT	12/15/04
10/526,988	CONTINUOUS EMULSIFICATION PROCESS FOR PROCESS CHEESE TYPE AND EQUIPMENT THEREFORE, AND CONTINUOUS PRODUCTION METHOD FOR PROCESS CHEESE TYPE AND EQUIPMENT THEREFOR	03/07/05
10/543,491	METHOD OF DETECTING BIFIDOBACTERIUM INFANTIS	07/26/05
10/548,927	PROCESS FOR PRODUCING CHEESE	09/12/05
10/562,384	CONTAINER, FROZEN MATERIAL PACKAGING BODY, AND METHOD OF MANUFACTURING PACKAGING BODY	12/27/05
10/564,302	**DRUG FOR CANCER THERAPY**	**01/10/06**
10/564,464	GLYCOSIDE HAVING 4-METHYLERGOST-7-EN-OL SKELETON AND HYPERGLYCEMIA IMPROVING AGENT	01/12/06
10/566,541	CHEWABLE CAPSULE AND PRODUCTION METHOD THEREOF	01/27/06
10/572,099	DRUG AND FOOD OR DRINK FOR IMPROVING HYPERGLYCEMIA	03/16/06
10/572,404	DRUG AND FOOD OR DRINK FOR IMPROVING HYPERGLYCEMIA	03/16/06
10/573,564	DRUG AND METHOD FOR PROLIFERATING NATURAL KILLER CELLS	03/27/06
11/580,173	INTERLEUKIN-18 INDUCER	10/12/06
11/576,652	DRUG AND FOOD OR DRINK FOR IMPROVING PANCREATIC FUNCTIONS	04/04/07
11/576,676	DRUG AND FOOD OR DRINK FOR IMPROVING PANCREATIC FUNCTIONS	04/04/07
11/577,301	DRUG AND FOOD OR DRINK FOR IMPROVING PANCREATIC FUNCTIONS	04/13/07
11/815,428	ALOE VERA EXTRACT, METHOD OF PRODUCING ALOE VERA EXTRACT, AND HYPERGLYCEMIA IMPROVING AGENT	08/02/07
11/913022	AGENT FOR INHIBITING VISCERAL FAT ACCUMULATION	29-Oct-2007
11/913758	AGENT FOR INHIBITING VISCERAL FAT ACCUMULATION	06-Nov-2007

11/916008	AGENT FOR IMPROVING INSULIN RESISTANCE	29-Nov-2007
11/917870	AGENT FOR IMPROVING INSULIN RESISTANCE	17-Dec-2007
11/994823	METHOD FOR DETECTION OF MICROORGANISM AND KIT FOR DETECTION OF MICROORGANISM	04-Jan-2008

CONCLUSION

In view of Applicants' amendments to the claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: Jan. 23, 2008

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